

CLAIMS

We claim:

1. A method for generating a secondary library of scaffold protein variants comprising:
  - 5 a) providing a primary library comprising a rank-ordered list of scaffold protein primary variant sequences;
  - b) generating a list of primary variant positions in said primary library;
  - c) combining a plurality of said primary variant positions to generate a secondary library of secondary sequences.
2. A method for generating a secondary library of scaffold protein variants comprising:
  - 10 a) providing a primary library comprising a rank-ordered list of scaffold protein primary variant sequences;
  - b) generating a probability distribution of amino acid residues in a plurality of variant positions;
  - c) combining a plurality of said amino acid residues to generate a secondary library of secondary sequences.
3. A method according to claim 1 further comprising synthesizing a plurality of said secondary sequences.
4. A method according to claim 2 wherein said synthesizing is done by multiple PCR with pooled oligonucleotides.
5. A method according to claim 4 wherein said pooled oligonucleotides are added in equimolar amounts.
6. A method according to claim 4 wherein said pooled oligonucleotides are added in amounts that correspond 20 to the frequency of the mutation.
7. A composition comprising a plurality of secondary variant proteins comprising a subset of said secondary library.
8. A composition comprising a plurality of nucleic acids encoding a plurality of secondary variant proteins comprising a subset of said secondary library.
- 25 9. A method for generating a secondary library of scaffold protein variants comprising:
  - a) providing a first library rank-ordered list of scaffold protein primary variants;
  - b) generating a probability distribution of amino acid residues in a plurality of variant positions;

c) synthesizing a plurality of scaffold protein secondary variants comprising a plurality of said amino acid residues to form a secondary library;  
wherein at least one of said secondary variants is different from said primary variants.